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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,491	12/05/2003	Jui H. Wang	11520.0338	9750
<div>26712      7590      11/06/2007</div> <div>HODGSON RUSS LLP THE GUARANTY BUILDING 140 PEARL STREET SUITE 100 BUFFALO, NY 14202-4040</div>				
			EXAMINER ZARA, JANE J	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 11/06/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/728,491

Applicant(s)

WANG ET AL.

Examiner

Jane Zara

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-33 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 26-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,7-25 and 31-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)         |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____   |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application          |
| Paper No(s)/Mail Date _____  | 6) <input checked="" type="checkbox"/> Other: <u>sequence alignments</u> . |

### **DETAILED ACTION**

The non-compliant amendment notice mailed 5-1-07 is hereby **VACATED** and an action on the merits is set forth below. The notice has been vacated because the misnumbering of the claims originated with the claim set filed 12-5-03, where claim 29 was omitted.

**The following amendments have been entered:**

Originally filed claims 30-34 are hereby renumbered as claims 29-33.

In originally filed claim 31, now renumbered as claim 30, "claim 30" in line 1 has been replaced with –claim 29--.

In originally filed claim 33, now renumbered as claim 32, "claim 32" in line 1 has been replaced with –claim 31--.

In originally filed claim 34, now renumbered as claim 33, "claim 32" in line 1 has been replaced with –claim 31--.

This Office action is in response to the communication filed 4-19-07.

Claims 1, 4-33 (previously numbered claims 1, 4-28 and 30-34) are pending in the instant application. Claims 6 and 26-30 are withdrawn as being drawn to non-elected inventions. Claims 1, 4, 5, 7-25 and 31-33, SEQ ID Nos. 1 and 20, have been examined on their merits as set forth below.

### ***Response to Arguments and Amendments***

*Withdrawn Rejections*

Any rejections not repeated in this office action are hereby withdrawn.

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

*New Rejections Necessitated by Amendments*

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 depends from claim 3, which has been canceled. Thus, the metes and bounds of claim 4 cannot be determined. Appropriate correction is required.

*New Rejections*

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 7-25 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Cho-Chung (USPN 5,271,941), Zhou et al (WO 99/50409), Agrawal (WO 97/11171) and Tsuchiya (WO 96/16967), in view of McKay et al (USPN 6,133,246) and Wang (USPN 5,858,988).

The claims are drawn to compositions and methods of reducing growth of cancer cells in vivo and down regulating expression of  $RI_{\alpha}$ /PKA in a cell comprising the administration of an oligoribonucleotide consisting of SEQ ID No. 1 or 20, between 21-23 nucleotides in length, and further comprising 2, 4-dinitrophenyl (DNP) at the 2'-O-position, which molar ratio of DNP to nucleotide is optionally between 0.5 to 0.8.

Cho-Chung (USPN 5,271,941) teaches antisense oligonucleotides between 21-23 nucleotides in length that target and inhibit the expression of  $RI_{\alpha}$ /PKA in cells in vitro and in vivo, and reduce cancer cell growth in vivo (See SEQ ID NO. 2 of Cho-Chung and the accompanying sequence alignment data between SEQ ID No. 2 of Cho-Chung and SEQ ID NO. 1 of the instant application; see also col. 9-16 and claims 1-21).

Zhou et al (WO 99/50409) teaches antisense oligonucleotides that target and inhibit the expression of  $RI_{\alpha}$ /PKA in cells (see Acc. No. AAZ30811 of Zhou and its alignment with SEQ ID NO. 1 of the instant application).

Agrawal (WO 97/11171) teaches antisense oligonucleotides between 15-30 nucleotides in length that target and inhibit the expression of  $RI_{\alpha}$ /PKA in cells and reduce cancer cell growth in vitro and in vivo. Agrawal also teaches 2'-O-modifications for enhancing antisense oligonucleotide stability and cellular uptake (See Acc. No. AAT64407 of Agrawal and the alignment data with SEQ ID NO. 1 of the instant application; see also pages 14-17, 39-42, 44, 45, claims 1, 5, 29, 30).

Tsuchiya (WO 96/16967) teaches antisense oligonucleotides between 15-30 nucleotides in length that target and inhibit the expression of  $RI_{\alpha}$ /PKA in cells (see Acc No. AAX34988 and its alignment with SEQ ID NO. 1 of the instant application).

McKay et al (USPN 6,133,246) teach methods of screening antisense oligonucleotides between 15-30 nucleotides in length for their ability to inhibit expression of a target gene of known sequence (see esp. col. 33-37, including tables 1 and 2).

Wang (USPN 5,858,988) teaches the enhancement of antisense oligonucleotide stability and cellular uptake in vitro and in vivo using antisense between 12-40 nucleotides in length and further comprising 2, 4-dinitrophenyl (DNP) at the 2'-O-position, including with a molar ratio of DNP to nucleotide of 0.5 to 0.8 (See esp. abstract, col. 7-8, 17-18, 23-28 and claims 1-63).

It would have been obvious to one of ordinary skill in the art to design and utilize an antisense oligonucleotide between 21-23 nucleotides in length and consistently of or comprising SEQ ID NO. 1 or 20 for targeting and inhibiting the expression of  $RI_{\alpha}$ /PKA in vitro or in vivo because antisense oligonucleotides in this size range, and directed to this particular target region of the target gene  $RI_{\alpha}$ /PKA have been routinely and successfully used for target gene inhibition of  $RI_{\alpha}$ /PKA, as taught previously by many in the art, including Cho-Chung, Zhou et al, Agrawal and Tsuchiya. One of ordinary skill in the art would have expected that the antisense nucleotide consisting of either SEQ ID NO. 1 or 20 would successfully target and inhibit the expression of  $RI_{\alpha}$ /PKA in vitro or in vivo because Cho-Chung, Zhou et al, Agrawal and Tsuchiya have demonstrated that using antisense in this size range and within the well known target subsequence region of SEQ ID No. 1 or 20 (e.g. within the well known target region of  $RI_{\alpha}$ /PKA) have successfully inhibited target gene expression in vitro and in vivo.

One of ordinary skill in the art would have been motivated to test various and obvious antisense oligonucleotides within this target region because this region's accessibility to antisense was well known in the art and designing a 21-23 nucleotide antisense within this target region would have been a design choice involving routine experimentation and relying on the combined teachings of Cho-Chung, Zhou et al, Agrawal and Tsuchiya in view of McKay et al. One of ordinary skill in the art would have had a reasonable expectation that SEQ ID NO. 1 or 20 would also inhibit tumor or cancer cell growth in vitro and in vivo because this had been illustrated previously with antisense oligonucleotides containing these subsequences and in this size range.

One of ordinary skill in the art would have used the routine experimentation taught previously by McKay to design particular subsequences of a well-known target region of a target gene for antisense inhibition. Furthermore, one of ordinary skill in the art would have been motivated to incorporate the well known modification of DNP into the 2'-O residues of antisense oligonucleotides because Wang had previously taught that this modification (in the molar range claimed) enhances antisense stability and target cell uptake. For these reasons the instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of

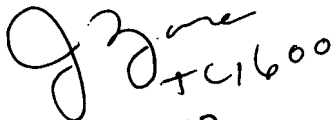


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a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**  
**10-31-07**

  
JANE ZARA, PH.D.  
PRIMARY EXAMINER